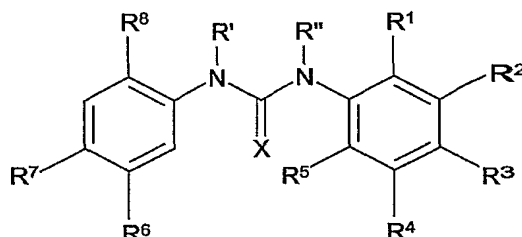


CLAIMS

1. A urea derivative represented by Formula I



any of its enantiomers or any mixture of its enantiomers, or a prodrug, or a pharmaceutically-acceptable addition salt thereof, wherein

X represents O, S or NR'''; wherein R''' represents hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl or cyano;

R' and R'', independently of each other, represent hydrogen, alkyl, cycloalkyl or cycloalkyl-alkyl;

R¹ represents hydrogen, alkyl, hydroxy, alkoxy, halo, haloalkyl, haloalkoxy, cyano, nitro, amino, or a group of formula -NR''''(CO)R''''', -NR''''(CO)Ar, -NR''''(CO)-NR''''R''''', -NR''''(CO)NR''''Ar, -NR''''(CO)CH=CH-R''''', -NR''''(SO₂)R'''''' or -NR''''(SO₂)Ar; wherein

R'''' and R''''', independently of each other, represent hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl, alkenyl, phenyl, or benzyl; and

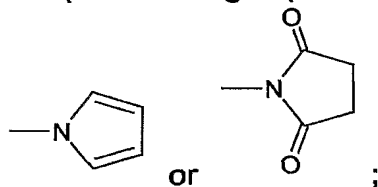
Ar represents an aryl group or an aromatic mono- or polycyclic heterocyclic group; or

R¹ represents a group of formula -CONR''''R'''''' or -SO₂-NR''''R'''''', wherein

R'''' and R''''', independently of each other, represent hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl, alkenyl, phenyl, or benzyl; or

R'''' and R'''''' together with the nitrogen atom to which they are attached form a heterocyclic ring; or

R¹ represents a group of formula



R² represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro or amino;

5 R³ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro or amino;

R⁴ represents hydrogen, alkyl, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro or amino;

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R⁵ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro or amino;

15 R⁶ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro, amino or phenyl;

R⁷ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro, amino or phenyl; and

20 R⁸ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, alkoxy, cyano, nitro or amino.

2. The urea derivative according to claim 1, wherein X represents O, S or NR'''; wherein R''' represents hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl or cyano.

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3. The urea derivative according to either one of claims 1-2, wherein R' and R'', independently of each other, represent hydrogen, alkyl, cycloalkyl or cycloalkyl-alkyl.

30 4. The urea derivative according to claim 3, wherein both of R' and R'' represent hydrogen.

5. The urea derivative according to any one of claims 1-4, wherein R¹ represents hydrogen, alkyl, hydroxy, alkoxy, halo, haloalkyl, haloalkoxy, cyano, nitro, amino, or a group of formula -NR''''(CO)R'''', -NR''''(CO)Ar, -NR''''(CO)-NR''''R'''', -NR''''(CO)NR''''Ar, -NR''''(CO)CH=CH-R'''', -NR''''(SO₂)R'''' or -NR''''(SO₂)Ar; wherein

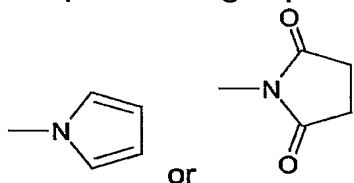
R'''' and R''''', independently of each other, represent hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl, alkenyl, phenyl or benzyl; and

Ar represents an aryl group or an aromatic mono- or polycyclic heterocyclic group; or

R^1 represents a group of formula $-\text{CONR}'''\text{R}''''$ or $-\text{SO}_2-\text{NR}'''\text{R}''''$, wherein R''' and R'''' , independently of each other, represent hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl, alkenyl, phenyl or benzyl; or

R''' and R'''' together with the nitrogen atom to which they are attached form a heterocyclic ring; or

R^1 represents a group of formula



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6. The urea derivative according to claim 5, wherein R^1 represents hydrogen, alkyl, hydroxy, alkoxy, halo, haloalkyl, haloalkoxy, cyano, nitro, amino, or a group of formula $-\text{NR}'''\text{(CO)R}''''$, $-\text{NR}'''\text{(CO)Ar}$, $-\text{NR}'''\text{(CO)-NR}'''\text{R}''''$, $-\text{NR}'''\text{(CO)NR}'''\text{Ar}$, $-\text{NR}'''\text{(CO)CH=CH-R}''''$, $-\text{NR}'''\text{(SO}_2\text{)R}''''$ or $-\text{NR}'''\text{(SO}_2\text{)Ar}$;

15 wherein

R''' and R'''' , independently of each other, represent hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl, alkenyl, phenyl or benzyl; and

Ar represents phenyl, pyrrolyl, imidazolyl, pyrazolyl or pyridinyl; or

R^1 represents a group of formula $-\text{CONR}'''\text{R}''''$ or $-\text{SO}_2-\text{NR}'''\text{R}''''$, wherein R''' and R'''' , independently of each other, represent hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl, alkenyl, phenyl or benzyl; or

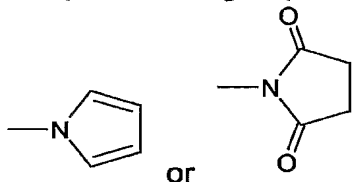
R''' and R'''' together with the nitrogen atom to which they are attached form a heterocyclic ring selected from pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl.

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7. The urea derivative according to claim 6, wherein R^1 represents hydrogen, alkyl, hydroxy, alkoxy, amino, or a group of formula $-\text{NR}'''\text{(CO)R}''''$; wherein

R''' and R'''' , independently of each other, represent hydrogen, alkyl, cycloalkyl, cycloalkyl-alkyl, alkenyl, phenyl or benzyl; or

R^1 represents a group of formula



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8. The urea derivative according to claim 6, wherein R¹ represents hydrogen, alkyl, hydroxy, alkoxy, amino, or -NH(CO)alkyl.

9. The urea derivative according to any one of claims 1-8, wherein R²
5 represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro or amino.

10. The urea derivative according to claim 9, wherein R² represents hydrogen, hydroxy or halo.

10 11. The urea derivative according to any one of claims 1-10, wherein R³ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro or amino.

12. The urea derivative according to claim 11, wherein R³ represents hydrogen, hydroxy, halo or nitro.

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13. The urea derivative according to any one of claims 1-12, wherein R⁴ represents hydrogen, alkyl, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro or amino.

14. The urea derivative according to claim 13, wherein R⁴ represents
20 hydrogen, alkyl or halo.

15. The urea derivative according to any one of claims 1-14, wherein R⁵ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro or amino.

25 16. The urea derivative according to claim 15, wherein R⁵ represents hydrogen, nitro or amino.

17. The urea derivative according to any one of claims 1-16, wherein R⁶ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro, amino or
30 phenyl.

18. The urea derivative according to claim 17, wherein R⁶ represents hydrogen, halo, haloalkyl or phenyl.

35 19. The urea derivative according to any one of claims 1-18, wherein R⁷ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, cyano, nitro, amino or phenyl.

20. The urea derivative according to claim 19, wherein R⁷ represents hydrogen, nitro or phenyl.

21. The urea derivative according to any one of claims 1-20, wherein R⁸ represents hydrogen, hydroxy, halo, haloalkyl, haloalkoxy, alkoxy, cyano, nitro or amino.

22. The urea derivative according to claim 21, wherein R⁸ represents hydrogen, hydroxy, halo or alkoxy.

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23. The urea derivative according to any one of claims 1-4, wherein R¹ represents hydrogen, alkyl, hydroxy, alkoxy, amino or -NH(CO)methyl; R² represents hydrogen, hydroxy or halo; R³ represents hydrogen, hydroxy, halo or nitro; R⁴ represents hydrogen, alkyl or halo; R⁵ represents hydrogen, alkyl, amino or nitro; R⁶ represents hydrogen, halo, haloalkyl or phenyl; R⁷ represents hydrogen or phenyl; and R⁸ represents hydrogen, hydroxy, halo or alkoxy.

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24. The urea derivative according to any one of claims 1-4, wherein R¹ represents hydroxy; R² represents hydrogen or halo; R³ represents hydrogen or nitro; R⁴ represents hydrogen or halo; R⁵ represents hydrogen, nitro or amino; R⁶ represents halo or haloalkyl; R⁷ represents hydrogen or phenyl; and R⁸ represents hydrogen, halo or alkoxy.

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25. The urea derivative according to any one of claims 1-4, wherein R¹ represents hydrogen; R² represents hydrogen, hydroxy or halo (chloro); R³ represents hydrogen or hydroxy; R⁴ represents alkyl or halo; R⁵ represents hydrogen; R⁶ represents hydrogen, haloalkyl or phenyl; R⁷ represents hydrogen or phenyl; and R⁸ represents hydrogen or halo.

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26. The urea derivative according to any one of claims 1–4, wherein

R^1 represents alkyl, alkoxy, amino or N-alkylcarbonyl-amino;

R^2 represents hydrogen;

5 R^3 represents hydroxy or halo;

R^4 represents hydrogen or halo;

R^5 represents hydrogen;

R^6 represents haloalkyl;

R^7 represents hydrogen; and

10 R^8 represents hydrogen or halo.

27. The urea derivative of claim 23, which is

N-(3-Chloro-6-hydroxy-phenyl)-*N'*-(2-chloro-5-trifluoromethyl-phenyl)-urea;

N-(2-Amino-6-hydroxy-phenyl)-*N'*-(3-trifluoromethyl-phenyl)-urea;

15 *N*-(5-Chloro-2-hydroxy-phenyl)-*N'*-(2-hydroxy-4-nitro-phenyl)-urea;

N-(2-Amino-4,5-dichloro-phenyl)-*N'*-(2-chloro-5-trifluoromethyl-phenyl)-

urea;

N-{4,5-Dichloro-2-[3-(2-chloro-5-trifluoromethyl-phenyl)-ureido]phenyl}-

acetamide;

20 *N*-(3-Chloro-4-hydroxy-phenyl)-*N'*-(3-trifluoromethyl-phenyl)-urea;

N-(4-Hydroxy-6-methyl-phenyl)-*N'*-(3-trifluoromethyl-phenyl)-urea;

N-(3,5-Dichloro-4-hydroxy-phenyl)-*N'*-(3-trifluoromethyl-phenyl) urea;

N-(2-Chloro-5-trifluoromethyl-phenyl)-*N'*-(3,5-dichloro-4-hydroxy-phenyl)

urea;

25 *N*-(Biphenyl-3-yl)-*N'*-(3,5-dichloro-4-hydroxy-phenyl) urea;

N-(Biphenyl-4-yl)-*N'*-(3,5-dichloro-4-hydroxy-phenyl) urea;

N-(Biphenyl-4-yl)-*N'*-(5-chloro-2-hydroxy-phenyl) urea;

N-(3,5-Dichloro-2-hydroxy-phenyl)-*N'*-(2-chloro-5-trifluoromethyl-phenyl)-

urea;

30 *N*-(3-Bromo-5-chloro-2-hydroxy-phenyl)-*N'*-(2-chloro-5-trifluoromethyl-phenyl)-urea;

N-(2-Chloro-5-trifluoromethyl-phenyl)-*N'*-(3-hydroxy-5-methyl-phenyl) urea;

N-(3-Hydroxy-5-methyl-phenyl)-*N'*-(3-trifluoromethyl-phenyl) urea;

N-(2-Chloro-5-trifluoromethyl-phenyl)-*N'*-(4-hydroxy-2-methyl-phenyl) urea;

35 *N*-(5-Chloro-2-methoxy-phenyl)-*N'*-(2-chloro-5-trifluoromethyl-phenyl) urea;

N-(2-Hydroxy-6-nitro-phenyl)-*N'*-(3-trifluoromethyl-phenyl) urea; or

N-(3-Chloro-6-methoxy-phenyl)-*N'*-(2-hydroxy-4-nitro-phenyl) urea;

or an enantiomer or a mixture of its enantiomers, or a pharmaceutically-acceptable addition salt thereof.

28. A pharmaceutical composition comprising a therapeutically effective amount of a urea derivative of any one of claims 1-27, or a pharmaceutically-acceptable addition salt thereof, together with at least one pharmaceutically-
5 acceptable carrier or diluent.

29. Use of a urea derivative of any one of claims 1-27, or a pharmaceutically-acceptable addition salt thereof, for the manufacture of a pharmaceutical composition/medicament for the treatment, prevention or alleviation of
10 a disease or a disorder or a condition of a mammal, including a human, which disease, disorder or condition is responsive to modulation of nicotinic acetylcholine $\alpha 7$ receptors.

30. The use according to claim 29, wherein the disease, disorder or
15 condition relates to the central nervous system.

31. The use according to claim 30, wherein the disease, disorder or condition is anxiety, cognitive disorders, learning deficit, memory deficits and dysfunction, Alzheimer's disease, attention deficit, attention deficit hyperactivity
20 disorder, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, Gilles de la Tourette's syndrome, depression, mania, manic depression, schizophrenia, obsessive compulsive disorders (OCD), panic disorders, eating disorders such as anorexia nervosa, bulimia and obesity, narcolepsy, nociception, AIDS-dementia, senile dementia, periferic neuropathy, autism, dyslexia, tardive
25 dyskinesia, hyperkinesia, epilepsy, bulimia, post-traumatic syndrome, social phobia, sleeping disorders, pseudodementia, Ganster's syndrome, pre-menstrual syndrome, late luteal phase syndrome, chronic fatigue syndrome, mutism, trichotillomania and jet-lag.

30 32. The use according to claim 29, wherein the disease, disorder or condition are associated with smooth muscle contractions, including convulsive disorders, angina pectoris, premature labour, convulsions, diarrhoea, asthma, epilepsy, tardive dyskinesia, hyperkinesia, premature ejaculation and erectile difficulty.

35 33. The use according to claim 29, wherein the disease, disorder or condition is related to the endocrine system, such as thyrotoxicosis, pheochromocytoma, hypertension and arrhythmias.

34. The use according to claim 29, wherein the disease, disorder or condition is a neurodegenerative disorders, including transient anoxia and induced neuro-degeneration.

5 35. The use according to claim 29, wherein the disease, disorder or condition is an inflammatory disorder, including inflammatory skin disorders such as acne and rosacea, Chron's disease, inflammatory bowel disease, ulcerative colitis and diarrhoea.

10 36. The use according to claim 29, wherein the disease, disorder or condition is mild, moderate or even severe pain of acute, chronic or recurrent character, as well as neuropathic pain and pain caused by migraine, postoperative pain, phantom limb pain, neuropathic pain, chronic headache, central pain, pain related to diabetic neuropathy, to post therapeutic neuralgia, or to peripheral nerve
15 injury.

 37. The use according to claim 29, wherein the disease, disorder or condition is associated with withdrawal symptoms caused by termination of use of addictive substances, including nicotine containing products such as tobacco, opioids
20 such as heroin, cocaine and morphine, benzodiazepines and benzodiazepine-like drugs and alcohol.

 38. A method of treatment, prevention or alleviation of a disease or a disorder or a condition of a living animal body, including a human, which disorder,
25 disease or condition is responsive to modulation of nicotinic acetylcholine $\alpha 7$ receptors, which method comprises the step of administering to such a living animal body in need thereof a therapeutically effective amount of a urea derivative of any one of claims 1-27.